

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A conjugate, comprising: a fluorophore or a photosensitizer, a quenching agent; and a targeting moiety, wherein: the fluorophore or the photosensitizer is linked to the quenching agent and the targeting moiety in such a way that activation of the fluorophore or the photosensitizer is quenched until the targeting moiety is bound to a target, whereupon the quenching agent remains linked through a non-cleavable linker but is displaced from the interaction-permissive energy transfer conformation with the photosensitizer, enabling activation of the photosensitizer upon irradiation with light of a suitable wavelength.

2. (Original) The conjugate of claim 1, wherein the fluorophore is 5-((2-aminoethyl)- amino) naphthalene-1-sulfonic acid (EDANS).

3. (Original) The conjugate of claim 1, wherein the photosensitizer is a porphyrin.

4. (Original) The conjugate of claim 1, wherein the photosensitizer is a chlorin.

5. (Original) The conjugate of claim 1, wherein the photosensitizer is a bacteriochlorin.

6. (Original) The conjugate of claim 1, wherein the quenching agent is β -carotene or a derivative thereof.

7. (Original) The conjugate of claim 1, wherein the targeting moiety is an antibody.

8. (Original) The conjugate of claim 1, wherein the targeting moiety is a fragment or other derivative of an antibody.

9. (Original) The conjugate of claim 1, wherein the targeting moiety is selected from the group consisting of an antigen, a ligand, a receptor, one member of a specific binding pair, a polyamide, a peptide, an oligosaccharide, a polysaccharide, a low density lipoprotein (LDL) or an apoprotein of LDL, a steroid, a steroid derivative, a hormone and a hormone-mimic.

10. (Original) The conjugate of claim 1, wherein the photosensitizer and the quenching agent include a linking component to link with an amino or hydroxy fatty acid or sulfonic acid of from 1 to 20 carbon atoms using ester, amide, or sulfonamide linkages.

11. (Original) The conjugate of claim 10, wherein the linking component is an oligonucleotide of 20-60 residues.

12. (Original) The conjugate of claim 11, wherein the oligonucleotide contains a specific sequence for binding to a desired target, along with at least one pair of mutually complementary regions that cause it to adopt a conformation, in the absence of the target, in which the quenching agent is sufficiently near to the photosensitizer to render it the photosensitizer inactive; wherein binding of the target-specific sequence to the target disrupts the conformation, allowing the photosensitizer to become active upon illumination with light of an appropriate wavelength.

13. (Original) The conjugate of claim 1, wherein the quenching agent is 4-(4'-dimethylamino- phenylazo) benzoic acid (DABCYL) or 4-(4'-dimethylamino-phenylazo) sulfonic (DABSYL).

14. (Original) The conjugate of claim 1, wherein the photosensitizer and quenching agent are linked by a polymer that exhibits binding specificity for the desired target, wherein in the absence of the target, the linked system adopts a conformation in which the quenching agent is sufficiently close to the photosensitizer to render it photochemically inert and wherein in the presence of the target, this conformation is disrupted, enabling photochemical processes to be carried out.

15. (Original) The conjugate of claim 1, wherein the photosensitizer comprises a porphyrin or porphyrin derivative tetrapyrrole and bears a physiologically acceptable metal atom in its central coordination cavity and one or more suitable functional groups are located on or near the quenching agent that efficiently coordinate to the axial position of the metal coordinated within the photosensitizer; and the targeting moiety is located in such a way that the presence of the target disrupts the relatively weak association of the axial ligand to the metal, releasing the quenching agent and rendering the fluorescent or PDT agent active.

16. (Original) The conjugate of claim 1, wherein the fluorophore emits light of a suitable wavelength for excitation of more than one type of secondary fluorophore or photosensitizer and the presence of more than one secondary fluorophore or photosensitizer allows the composition to produce different responses, designed to be appropriate to the presence of each of the targets with which the composition can react.

17. (Original) The conjugate of claim 1, wherein the targeting moiety is a polymer bearing at least one sulfate or sulfonate functional group.

18. (Original) The conjugate of claim 17, wherein the targeting moiety is dextran sulfate.

19. (Original) The conjugate of claim 18, wherein the dextran sulfate has an average molecular weight of about 5,000.

20. (Original) The conjugate of claim 1, wherein the photosensitizer is Talaporfin sodium.

21. (Original) A pharmaceutical composition, comprising the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof in a pharmaceutically acceptable carrier.

22. (Original) An article of manufacture, comprising: packaging material; and the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof contained within the packaging material, wherein: the conjugate or pharmaceutically acceptable derivative thereof is effective in a photodynamic therapy treatment for ameliorating the symptoms of a hyperproliferative disorder; and the packaging material includes a label that indicates that the composition or salt thereof is used in a photodynamic therapy treatment for ameliorating the symptoms of a hyperproliferative disorder.

23. (Original) A method for administering a photodynamic therapy to a target, comprising: (i) administering to a subject a conjugate of claim 1 or a pharmaceutically acceptable derivative thereof that preferentially associates with the target; and (ii) irradiating the subject with light of a wavelength and total fluence sufficient to produce a therapeutic effect.

24. (Original) The method of claim 23, wherein the target is selected from the group consisting of a vascular endothelial tissue, a neovasculature tissue, a neovasculature tissue present in an eye, an abnormal vascular wall of a tumor, a solid tumor, a tumor of a head, a

tumor of a neck, a tumor of an eye, a tumor of a gastrointestinal tract, a tumor of a liver, a tumor of a breast, a tumor of a prostate, a tumors of a lung, a nonsolid tumor, malignant cells of one of a hematopoietic tissue and a lymphoid tissue, lesions in a vascular system, a diseased bone marrow, and diseased cells in which the disease is one of an autoimmune and an inflammatory disease.

25. (Original) The method of claim 24, wherein the target composition is selected from the group consisting of bacteria, viruses, fungi, protozoa, and toxins.

26. (Original) The method of claim 24, further comprising the step of allowing sufficient time for any of the conjugate that is not preferentially associated to the target to clear from non-target tissue of the subject prior to the step of irradiating.

27. (Original) A method of photodynamic therapy for treating hyperproliferative tissue in a subject, comprising: (i) administering to the subject the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof that preferentially associates with the hyperproliferative tissue, and (ii) irradiating the subject with light of a wavelength and fluence sufficient to activate the conjugate, whereby the hyperproliferative tissue is destroyed or impaired.

28. (Original) A method for detecting the presence of a target tissue in a subject comprising: (i) administering to the subject a sufficient quantity of the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof that preferentially associates with the target tissue; and (ii) visualizing the conjugate within the patient.

29. (Original) The method of claim 28 wherein the step of visualizing is accomplished by exposing the conjugate with light of sufficient energy to cause the composition to fluoresce.

30. (Original) A method for detecting a target in a biological sample, comprising: (i) adding to the biological sample the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof that binds to the target; and (ii) detecting the composition.

31. (Original) The method of claim 32, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial fluid, sweat, interstitial fluid, sperm, cerebrospinal fluid, ascites fluid, and/or tumor tissue biopsy and circulating tumor cells.

32. (Original) A method of diagnosing an infecting agent in a patient, comprising: (i) administering to the patient the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof having a targeting moiety that binds to the infecting agent; and (iii) visualizing the conjugate within the patient.

33. (Original) The method of claim 32 wherein the step of visualizing is accomplished by exposing the conjugate with light of sufficient energy to cause the conjugate to fluoresce.

34. (Original) A method of generating an image of a target tissue or target composition in a subject, comprising: (i) administering to the subject the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof; and (ii) generating an image of at least a part of the subject to which the conjugate has preferentially associated.

35. (Original) A kit to treat hyperproliferative disorders, comprising the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof and instructions teaching a method of photodynamic therapy.

36. (Original) A kit to specifically label a cell or tissue, comprising: the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof comprising a targeting

moiety directed to the specific cell or tissue; and instructions teaching a method of fluorescence imaging.

37. (Original) A combination, comprising: the conjugate of claim 1 or a pharmaceutically acceptable derivative thereof; and a light source.

38. (Original) A conjugate, comprising: a tetrapyrrole or tetrapyrrole derivative photosensitizer that comprises a physiologically acceptable metal atom in its central coordination cavity; a quenching agent comprising one or more suitable functional groups that coordinate to the axial position of the metal coordinated within the photosensitizer and position the quenching agent in an energy transfer conformation with the photosensitizer so that activation of the photosensitizer is quenched; and a targeting moiety, wherein binding of the targeting moiety to a target disrupts the association of the axial ligand of the quenching agent to the metal, releasing the quenching agent and rendering the photosensitizer active.

39. (Original) The conjugate of claim 38, wherein the photosensitizer is a porphyrin.

40. (Original) The conjugate of claim 38, wherein the photosensitizer is a chlorin.

41. (Original) The conjugate of claim 38, wherein the photosensitizer is a bacteriochlorin.

42. (Original) The conjugate of claim 38, wherein the photosensitizer is Talaporfin sodium.

43. (Original) The conjugate of claim 38, wherein the quenching agent is 0-carotene or a derivative thereof.

44. (Original) The conjugate of claim 38, wherein the targeting moiety is an antibody, and antibody fragment or other derivative of an antibody.

45. (Original) The conjugate of claim 38, wherein the targeting moiety is selected from the group consisting of an antigen, a ligand, a receptor, one member of a specific binding pair, a polyamide, a peptide, an oligosaccharide, a polysaccharide, a low density lipoprotein (LDL) or an apoprotein of LDL, a steroid, a steroid derivative, a hormone and a hormone-mimic.

46. (Original) The conjugate of claim 38, wherein the targeting moiety is dextran sulfate.

47. (Original) The conjugate of claim 38, wherein the quenching agent is 4-(4'-dimethylamino- phenylazo) benzoic acid (DABCYL) or 4-(4'-dimethylamino-phenylazo) sulfonic (DABSYL).

48. (Original) A pharmaceutical composition, comprising the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof in a pharmaceutically acceptable carrier.

49. (Original) An article of manufacture, comprising: packaging material; and the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof contained within the packaging material, wherein: the conjugate or pharmaceutically acceptable derivative thereof is effective in a photodynamic therapy treatment for ameliorating the symptoms of a hyperproliferative disorder; and the packaging material includes a label that indicates that the composition or salt thereof is used in a photodynamic therapy treatment for ameliorating the symptoms of a hyperproliferative disorder.

50. (Original) A method for administering a photodynamic therapy to a target, comprising: (i) administering to a subject a conjugate of claim 38 or a pharmaceutically acceptable derivative thereof that preferentially associates with the target; and (ii) irradiating the subject with light of a wavelength and total fluence sufficient to produce a therapeutic effect.

51. (Original) The method of claim 50, wherein the target is selected from the group consisting of a vascular endothelial tissue, a neovasculature tissue, a neovasculature tissue present in an eye, an abnormal vascular wall of a tumor, a solid tumor, a tumor of a head, a tumor of a neck, a tumor of an eye, a tumor of a gastrointestinal tract, a tumor of a liver, a tumor of a breast, a tumor of a prostate, a tumors of a lung, a nonsolid tumor, malignant cells of one of a hematopoietic tissue and a lymphoid tissue, lesions in a vascular system, a diseased bone marrow, and diseased cells in which the disease is one of an autoimmune and an inflammatory disease.

52. (Original) The method of claim 50, wherein the target composition is selected from the group consisting of bacteria, viruses, fungi, protozoa, and toxins.

53. (Original) The method of claim 50, further comprising the step of allowing sufficient time for any of the conjugate that is not preferentially associated to the target to clear from non-target tissue of the subject prior to the step of irradiating.

54. (Original) A method of photodynamic therapy for treating hyperproliferative tissue in a subject, comprising: (i) administering to the subject the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof that preferentially associates with the hyperproliferative tissue, and (ii) irradiating the subject with light of a wavelength and fluence sufficient to activate the conjugate, whereby the hyperproliferative tissue is destroyed or impaired.

55. (Original) A method for detecting the presence of a target tissue in a subject comprising: (i) administering to the subject a sufficient quantity of the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof that preferentially associates with the target tissue; and (ii) visualizing the conjugate within the patient.

56. (Original) The method of claim 55 wherein the step of visualizing is accomplished by exposing the conjugate with light of sufficient energy to cause the composition to fluoresce.

57. (Original) A method for detecting a target in a biological sample, comprising: (i) adding to the biological sample the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof that binds to the target ; and (ii) detecting the composition.

58. (Original) The method of claim 57, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial fluid, sweat, interstitial fluid, sperm, cerebrospinal fluid, ascites fluid, and/or tumor tissue biopsy and circulating tumor cells.

59. (Original) A method of diagnosing an infecting agent in a patient, comprising: (i) administering to the patient the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof having a targeting moiety that binds to the infecting agent; and (iii) visualizing the conjugate within the patient.

60. (Original) The method of claim 59 wherein the step of visualizing is accomplished by exposing the conjugate with light of sufficient energy to cause the conjugate to fluoresce.

61. (Original) A method of generating an image of a target tissue or target composition in a subject, comprising: (i) administering to the subject the conjugate of claim 38

or a pharmaceutically acceptable derivative thereof; and (ii) generating an image of at least a part of the subject to which the conjugate has preferentially associated.

62. (Original) A kit to treat hyperproliferative disorders, comprising the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof and instructions teaching a method of photodynamic therapy.

63. (Original) A kit to label specific a cell or tissue, comprising: the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof comprising a targeting moiety directed to the specific cell or tissue; and (') instructions teaching a method of fluorescence imaging.

64. (Original) A combination, comprising: the conjugate of claim 38 or a pharmaceutically acceptable derivative thereof; and a light source.